

**WHAT IS CLAIMED IS: -**

1. A method for promoting the survival of a stem cell in culture, comprising culturing said cell in the presence of a myeloproliferative receptor (mpl) ligand, wherein said ligand binds mpl and mpl-mediated biological activity is initiated.
2. The method of claim 1, wherein said mpl ligand is thrombopoietin.
3. The method of claim 2, wherein said thrombopoietin is human thrombopoietin.
4. The method of claim 3, wherein said thrombopoietin is recombinant human thrombopoietin.
5. The method of claim 1, wherein said cell cultured in the presence of said mpl ligand is characterized by the capability of self-renewal and ability to give rise to all hematopoietic cell lineages.
6. The method of claim 1, wherein said cell is a human stem cell.
7. The method of claim 6, wherein said cell is  $CD34^{+}$ .
8. The method of claim 6, wherein said cell is  $CD34^{+}Lin^{-}$ .
9. The method of claim 6, wherein said cell is  $CD34^{+}Thy^{+}Lin^{-}$ .
10. The method of claim 6, wherein said cell is  $CD34^{+}Lin^{-}Rho^{lo}$  or  $CD34^{+}Thy^{+}Lin^{-}Rho^{lo}$ .
11. The method of claim 4, wherein said recombinant human thrombopoietin is present in a concentration of about 1 ng/ml to about 100 ng/ml.
12. A method of expanding a population of stem cells, comprising exposing a stem cell to a mpl ligand, wherein said cell proliferates to form an expanded population of stem cells.

13. The method of claim 12, wherein said mpl ligand is thrombopoietin.
14. The method of claim 13, wherein said thrombopoietin is human thrombopoietin.
15. The method of claim 14, wherein said thrombopoietin is recombinant human thrombopoietin.
16. The method of claim 12, wherein said expanded cell population is characterized by the ability to undergo substantial self-renewal and ability to give rise to all hematopoietic cell lineages.
17. The method of claim 12, wherein said cells are human stem cells.
18. The method of claim 17, wherein said cell is CD34<sup>+</sup>.
19. The method of claim 17, wherein said cell is CD34<sup>+</sup>Lin<sup>-</sup>.
20. The method of claim 17, wherein said cell is CD34<sup>+</sup>Thy<sup>+</sup>Lin<sup>-</sup>.
21. The method of claim 17, wherein said cell is CD34<sup>+</sup>Lin<sup>-</sup>Rho<sup>lo</sup> or CD34<sup>+</sup>Thy<sup>+</sup>Lin<sup>-</sup>Rho<sup>lo</sup>.
22. The method of claim 15, wherein said recombinant human thrombopoietin is present in a concentration of about 1 ng/ml to about 100 ng/ml.
23. A therapeutic method for restoring hematopoietic capability to a human subject, said method comprising the steps of:
  - (a) removing stem cells from a human subject;
  - (b) expanding said cells in the presence of a mpl ligand to form an expanded population of stem cells from a human subject; and
  - (c) returning said expanded cells to said subject, wherein hematopoietic capability is restored to said patient.

24. The method of claim 23, wherein said expanded population of stem cells are characterized by the capability of self-renewal and ability to give rise to all hematopoietic cell lineages.
25. The method of claim 23, wherein said mpl ligand is thrombopoietin.
26. The method of claim 23, wherein said thrombopoietin is human thrombopoietin.
27. The method of claim 26, wherein said thrombopoietin is recombinant human thrombopoietin.
28. The method of claim 27, wherein said recombinant human thrombopoietin is present in a concentration of about 1 ng/ml to about 100 ng/ml.
29. The method of claim 24, wherein said cells are expanded in the presence of one or more additional cytokines.
30. The method of claim 29, wherein said cytokines are selected from the group consisting of interleukin 3 (IL-3), interleukin 6 (IL-6), leukemia inhibitory factor (LIF), c-kit ligand (KL), granulocyte-macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), and steel factor (Stl).
31. The method of claim 30, wherein said cytokine is IL-3.
32. A method for activating a quiescent stem cell to divide, comprising exposing said quiescent cell to a mpl ligand, wherein said cell is activated to divide.
33. The method of claim 32, wherein said mpl ligand is thrombopoietin.
34. The method of claim 33, wherein said thrombopoietin is human thrombopoietin.
35. The method of claim 34, wherein said thrombopoietin is recombinant human thrombopoietin.

36. The method of claim 32, wherein said cell is a human stem cell.
37. The method of claim 36, wherein said cell is CD34<sup>+</sup>.
38. The method of claim 36, wherein said cell is CD34<sup>+</sup>Lin<sup>-</sup>.
39. The method of claim 36, wherein said cell is CD34<sup>+</sup>Thy<sup>+</sup>Lin<sup>-</sup>.
40. The method of claim 36, wherein said cell is CD34<sup>+</sup>Lin<sup>-</sup>Rho<sup>lo</sup> or CD34<sup>+</sup>Thy<sup>+</sup>Lin<sup>-</sup>Rho<sup>lo</sup>.
41. The method of claim 32, wherein cells formed from said activated cell are characterized by the capability of self-renewal and ability to give rise to all hematopoietic cell lineages.
42. The method of claim 35, wherein said recombinant human thrombopoietin is present in the concentration range of about 1 ng/ml to about 100 ng/ml.
43. A method for modifying a stem cell, comprising the steps of:
- (a) inserting a foreign gene into a viral vector;
  - (b) culturing a quiescent stem cell in the presence of a mpl ligand, wherein said cell is activated to divide; and
  - (c) exposing said activated cell to said viral vector, wherein said foreign gene is integrated into the DNA of said stem cell.
44. The method of claim 43, wherein said mpl ligand is thrombopoietin.
45. The method of claim 44, wherein said thrombopoietin is human thrombopoietin.
46. The method of claim 45, wherein said thrombopoietin is recombinant human thrombopoietin.
47. A method for providing gene therapy to a subject, comprising providing the modified stem cell of claim 43 to a subject in need thereof.

48. The method of claim 31, wherein said foreign gene encodes a protein selected from the group consisting of the *mdr1* gene product, adenosine deaminase, glucocerebrosidase,  $\beta$ -globin, Factor VIII, Factor IX, *mdr* related protein, T-cell receptors, and cytokines.
49. The method of claim 31, wherein said foreign gene is an antisense or ribozyme sequence.
50. The method of claim 43, wherein said thrombopoietin is a thrombopoietin mimetic.
51. The method of claim 43, wherein said viral vector is a retroviral vector.
52. The method of claim 43, further comprising the steps of:
- transplanting said final cell population into a recipient to provide long term hematopoietic reconstitution.
53. The method of claim 52, wherein said initial hematopoietic cell population is obtained from said recipient.
54. The method of claim 52, further comprising the step of selecting CD34<sup>+</sup> cells from said final population prior to said transplanting step.
55. The method of claim 54, wherein said selecting step further selects cells from said final population that are Thy-1<sup>+</sup>.
56. The method of claim 45, wherein said human thrombopoietin is present in a concentration of about 1 ng/ml to about 100 ng/ml.
57. The method of claim 50, wherein said thrombopoietin mimetic is present in a concentration of about 1 ng/ml to about 100 ng/ml.

58. The method of claim 43, wherein said medium further comprises at least one cytokine selected from the group consisting of interleukin 3 (IL-3), interleukin 6 (IL-6), leukemia inhibitory factor (LIF), c-kit ligand (KL), granulocyte-macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF) and fetal liver kinase 2 (FLK-2) ligand.

59. The method of claim 43, wherein said initial population of cells is selected for positive expression of CD34 prior to said culturing step.

60. The method of claim 43, wherein said gene of interest encodes a protein selected from the group consisting of the *mdr1* gene product, adenosine deaminase, glucocerebrosidase,  $\beta$ -globin, Factor VIII, Factor IX, *mdr* related protein, T-cell receptors, and cytokines.

61. The method of claim 43, wherein said gene of interest is an antisense or ribozyme sequence.

62. The method of claim 43, wherein said retrovirus is an amphotropic retrovirus.